REMARKS

The Examiner has rejected claims 1-8 under 35 U.S.C 103(a) as being unpatentable over the Salvesen et al. reference in light of STN Registry File No. 17590-01-1 and Stedman's Medical Dictionary (Twenty-Second Edition, 1972; p.377) each cited to show facts, in view of Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980; ppp.420-426).

The Salvesen reference shows that the amphetaminil racemate has a general stimulant effect and that four stereoisomeric configurations exist as identified by chromatographic separation and isolated from thin layer chromatography spots. The Examiner argues that it would be reasonable to expect that one of the stereoisomers would provide optimal therapeutic effects and that it would be predictable to purify such a stereoisomer.

In re May, 574 F.2d 1082, 1090-94 (C.C.P.A. 1978) held a stereoisomer nonobvious over the racemic mixture of stereoisomer, because the isolated stereoisomer was unexpectedly nonaddictive. On the other hand, In re Adamson, 275 F.2d 952, 954-55 (C.C.P.A. 1960) held that an isolated stereoisomer was obvious over the racemic mixture of isomers given insufficient showing of any unexpected result.

Applicants have shown that (R,R'),(R,S')-amphetaminil is more effective as a stimulant and has fewer movement-related side effects compared with the racemate which is an unexpected result. Applicants contend that such results are not at all predictable. Resolved isomers have been found to be of equal therapeutic effect, have been found to have different biological activities, and some are inactive. Frequently, the isolated isomers show a less optimal therapeutic effect compared with the racemate. There are many variables to determine the effect of an isomer, including the structure of the compound, the receptors of the isomers, the disease to be treated, the toxicity of the isomer, the metabolism of the isomer, the bioavailability of the isomer and the stability of the isomer. The compounds may have different pharmacodynamic, pharmacokinetic and pharmacological properties making difficult to predict their effectiveness as therapeutic products.

The composition of the invention not only has an optimal therapeutic effect but also lacks potentially dangerous side effects associated with the administration of the racemate. The invention shows a greater stimulant effect compared with the racemate and fewer stereotypy-associated side effects. Therefore the simultaneous increase in activity and decrease in toxicity is surprisingly and unexpectedly advantageous. A skilled artisan would have expected the exact opposite, ie that a compound's toxicity would increase with its increased therapeutic effect.

These are not predictable results. Furthermore, the Applicants spent a considerable amount of time attempting to purify the isomers and had issues of degradation whenever the isomers were isolated. The fact that the isolated stereoisomers are less stable than the racemate points to the unpredictablity of characterizing the properties of stereoisomers based on the properties of the racemate.

In view of the above, Applicants do not believe the Salvesen reference predicts, teaches, suggests or motivates the present invention either in light of STN Registry File No. 17590-01-1 which shows the structure of amphetaminil and or in light of Stedman's Medical Dictionary which shows that dragees are sugar-coated pills or capsules, or in light of Remington's Pharmaceutical Sciences which shows that drugs are chemically modified to alter the duration of action of a drug; to modify the transportation and distribution of the drug in the body; to reduce toxicity; and to overcome difficulties encountered in pharmaceutical formulation procedures or in the dosage form itself.

Applicants believe that the claimed invention is patentably distinct from the references cited by the Examiner and that the foregoing remarks place the claims in condition for allowance. No new matter has been introduced by these amendments. No fees are believed due for the filing of this paper.

Any questions about this response should be addressed to Karen Guerrero. The telephone number is 610-933-2490.

Sincerely,

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